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ORIGINAL ARTICLE

Prompt healing of erosive oral lichen planus lesion after combined corticosteroid treatment with locally injected triamcinolone acetonide plus oral prednisolone

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KEYWORDS
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Background/Purpose: Erosive oral lichen planus (EOLP) is a T-cell-mediated inflammatory disease that is refractory to treat. This study tested whether local injection of triamcinolone acetonide plus oral administration of low- or medium-dose prednisolone could hasten the healing of EOLP lesions.
Methods: In this study, 50 EOLP patients were treated with local injection of Kenacort A (40 mg triamcinolone acetonide once weekly for 3 and 2 weeks for 30 major and 20 minor EOLP patients, respectively) plus oral administration of prednisolone (25–30 mg and 15–20 mg of prednisolone once daily for 2 weeks for 30 major and 20 minor EOLP patients, respectively). The oral administration of prednisolone was tapered to 5 mg per day and stopped in 7 days. Then, the patients were treated with topical Dexaltin (0.1% dexamethasone, once or twice per daily) and oral administration of vitamin Bc (one capsule twice daily) thereafter.
Results: After 3-week treatments, the 30 major EOLP patients showed complete response (lack of detectable erosive or ulcerative lesion with absence or regression of reticular or papular OLP) in 27 cases (90%) and partial response (reduction of erosive or ulcerative lesion by at least 30% in diameter with regression of reticular or papular OLP) in cases (10%); and 20 minor EOLP patients demonstrated complete response in 18 cases (90%) and partial response in two cases (10%). However, all the 45 complete response major or minor EOLP patients showed recurrence of erosive or ulcerative lesion after 3–24 (mean 12) months of follow-up.
Conclusion: Prompt and complete healing of the EOLP lesions could be achieved in a relative short period of time after treatment with our protocol. Although complete response EOLP

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lesions recurred after a follow-up period of 3—24 months, patients did have an average remission period of 12 months after treatment with our protocol.

Introduction

Oral lichen planus (OLP) is a chronic inflammatory oral mucosal disease. Both antigen-specific and nonspecific mechanisms are involved in the pathogenesis of OLP. Antigen-specific mechanisms include antigen presentation by basal keratinocytes and antigen-specific keratinocyte killing by $CD8^+$ cytotoxic T lymphocytes. Nonspecific mechanisms include mast cell degranulation and matrix metalloproteinase activation in OLP lesions.[1,2] Through mast cell/T-cell interactions in OLP lesions, mast cell-released cytokines, chemokines and matrix metalloproteinases can promote T-cell activation, migration, proliferation and differentiation.[3] OLP is histologically characterized by liquefaction degeneration of basal epithelial cells and an intraepithelial and subepithelial infiltrate of $CD8^+$ cells in the superficial lamina propria. $CD4^+$ cells are observed mainly in the deep lamina propria.[4] An increase in histocompatibility leukocyte antigen (HLA)-DR-positive $CD3^+$ cells in both the local lesional tissues and peripheral lymphocytes also indicates T-cell activation in OLP.[5,6] The above findings suggest that OLP is a T-cell-mediated inflammatory disease.

Clinically, patients with the reticular, papular or plaque type of OLP usually have minor or no symptoms, but patients with erosive OLP (EOLP) often have significant symptoms of pain and a burning sensation at the oral mucosa. Therefore, the most important aim of EOLP treatment is to promote the healing of erosive or ulcerative oral mucosal lesions. This study tested whether local injection of 40 mg triamcinolone acetonide once weekly for 2—3 weeks plus oral administration of 15—30 mg prednisolone once daily for 2 weeks could hasten the healing of EOLP lesions and allow the OLP patients to obtain a relatively long period of lesion remission.

Materials and methods

Subjects

The study group consisted of 50 EOLP patients (seven men and 43 women, age range 29—78 years, mean 54.8 years) without LP of other mucosal or skin surfaces. All the patients were seen consecutively, diagnosed, and treated in the Department of Oral Diagnosis of National Taiwan University Hospital from July 2005 to June 2008. OLP patients with areca quid chewing habit, hypertension, and autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, Sjögren's syndrome, pemphigus vulgaris, and cicatricial pemphigoid were excluded. In addition, none of the patients had taken any prescription medication for at least 3 months before entering the study. Patients were selected according to the following criteria: (1) a typical clinical presentation of radiating grayish-white Wickham striae or papules combined with erosion or ulceration on the bilateral posterior buccal or vestibular mucosa; and (2) biopsy specimens characteristic of OLP, that is, hyperkeratosis or parakeratosis, a slightly acanthotic epithelium with liquefaction degeneration of the basal epithelial cells, a pronounced band-like lymphocytic infiltrate in the lamina propria, and the absence of epithelial dysplasia. The EOLP was further divided into the major (30 patients with erosive or ulcerative lesions $\geq$ 1 cm in diameter) and minor types (20 patients with erosive or ulcerative lesions $<$ 1 cm in diameter) according to criteria described previously.[7]

After pathological diagnosis was confirmed, the 50 EOLP patients were treated with a local injection of 40 mg Kenacort A (triamcinolone acetonide) that was dissolved in 2 mL injection water and injected into the submucosa of the erosive or ulcerative OLP lesions at the bilateral posterior buccal or vestibular mucosa (1 mL for each side of lesion). The local injection was performed once weekly for 2 (for minor EOLP patients) or 3 weeks (for major EOLP patients). In addition, oral administration of 15—20 mg of prednisolone (for minor EOLP patients) or 25—30 mg of prednisolone (for major EOLP patients) once daily was given to each patient for 2 weeks. The oral administration of prednisolone was tapered to 5 mg per day and stopped in 7 days. Then, the patients were treated with topical Dexaltin (0.1% dexamethasone, once or twice daily) and oral vitamin Bc (one capsule twice daily) thereafter. The patients were examined once a week for 4 weeks and then once a month thereafter. Clinical photographs were taken at each patient visit for evaluation of lesion progression or regression. Lesion response was evaluated with special regard to the erosive or ulcerative lesions and characterized as follows: complete response, lack of detectable erosive or ulcerative lesion with absence or regression of reticular or papular OLP confirmed by clinical evaluation; partial response, reduction of erosive or ulcerative lesion by at least 30% in diameter with regression of reticular or papular OLP; and no response, reduction of erosive or ulcerative lesion by less than 30% in diameter with regression of reticular or papular OLP. All lesion responses were evaluated at the completion of the 3-week treatment. The duration of recurrence was measured from the end of the 3-week treatment to the time of recurrence. This study was reviewed and approved by the Institutional Review Board at the National Taiwan University Hospital.

Results

In this study, 50 EOLP patients were treated with local injection of Kenacort A (40 mg triamcinolone acetonide once weekly for 3 and 2 weeks for 30 major and 20 minor EOLP patients, respectively) plus oral prednisolone

(25—30 mg and 15—20 mg prednisolone once daily for 2 weeks for 30 major and 20 minor EOLP patients, respectively). After the 3-week treatments, the 30 major EOLP patients showed complete response in 27 cases (90%) (Fig. 1) and partial response in three cases (10%); and the 20 minor EOLP patients demonstrated complete response in 18 cases (90%) (Fig. 2) and partial response in two cases (10%) (Table 1). The EOLP patients were then treated with topical Dexaltin once or twice daily and oral vitamin Bc (one capsule twice daily) 3 weeks later. All the 27 complete response major EOLP patients showed recurrence of erosive or ulcerative lesion after 3—24 (mean 12 ± 5) months of follow-up. In addition, all the 18 complete response minor EOLP patients demonstrated recurrence of erosive or ulcerative lesion after 3—24 (mean 12 ± 6) months of follow-up (Table 2). The recurrence EOLP patients were treated with the same protocol (local injection plus oral administration of corticosteroid) as before and the majority of the patients could achieve complete response after receiving the same treatment modality (data not shown).

Discussion

This study found that 90% of erosive or ulcerative OLP lesions could show complete regression after 2—3 weeks of treatment with local injection of triamcinolone acetonide plus oral administration of low- or medium-dose prednisolone for 2 weeks. This suggests that a prompt and complete healing of the erosive or ulcerative EOLP lesions can be achieved in a relative short period of 2—3 weeks after treatment with our protocol. However, the EOLP lesion did recur 3—24 (mean 12) months after complete response of the lesion had been achieved. By asking the patients, the recurrence of the EOLP lesions was usually elicited by episodes such as insomnia for a few days, a common cold, a great emotional disturbance, or a sudden disaster within the family.

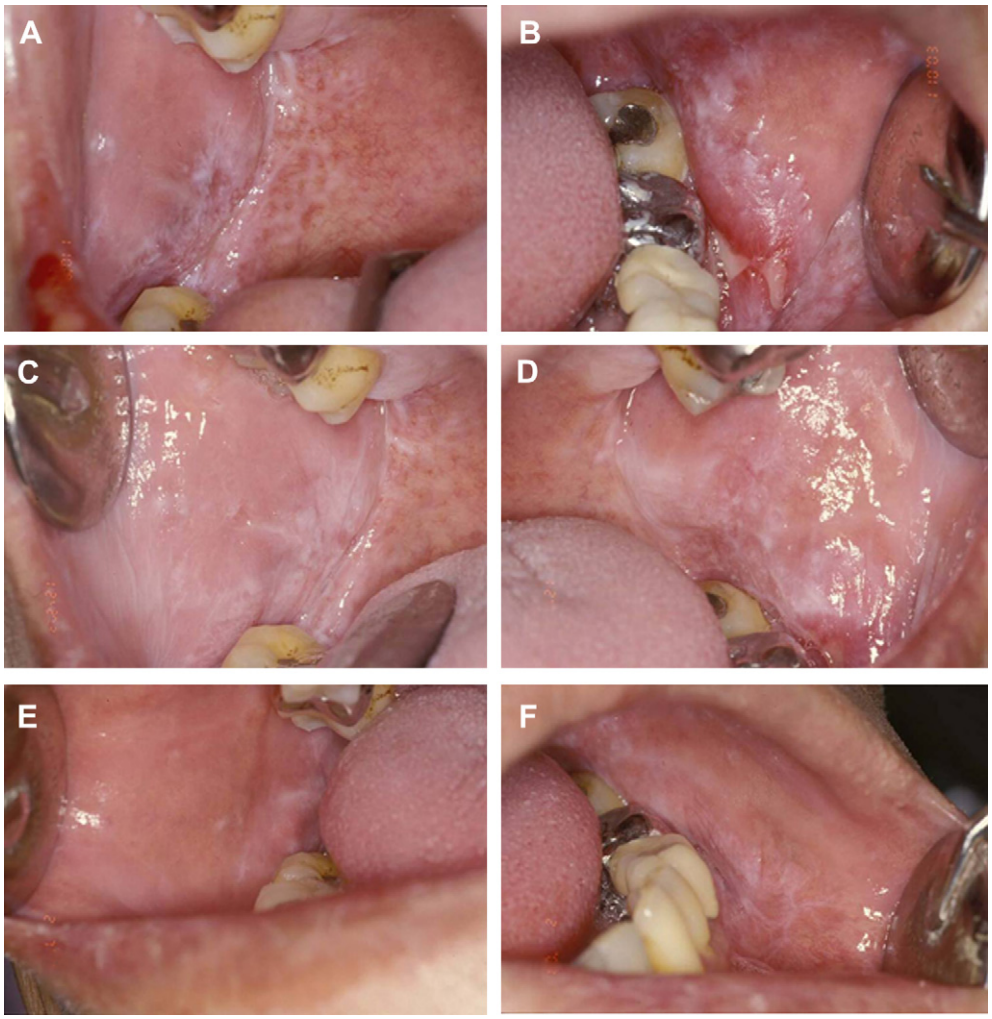

Figure 1 Clinical photographs of a patient with major-type erosive oral lichen planus (EOLP) on the bilateral posterior buccal mucosa. (A and B) Before treatment. (C and D) After one round of local injection of 40 mg triamcinolone acetonide once weekly plus oral administration of 25 mg prednisolone once daily for 1 week, showing partial response of the lesion. (E and F) After two rounds of local injection of 40 mg triamcinolone acetonide once weekly plus oral administration of 25 mg prednisolone once daily for 2 weeks, showing complete healing of the ulcerative lesion with residual reticular-type oral lichen planus.

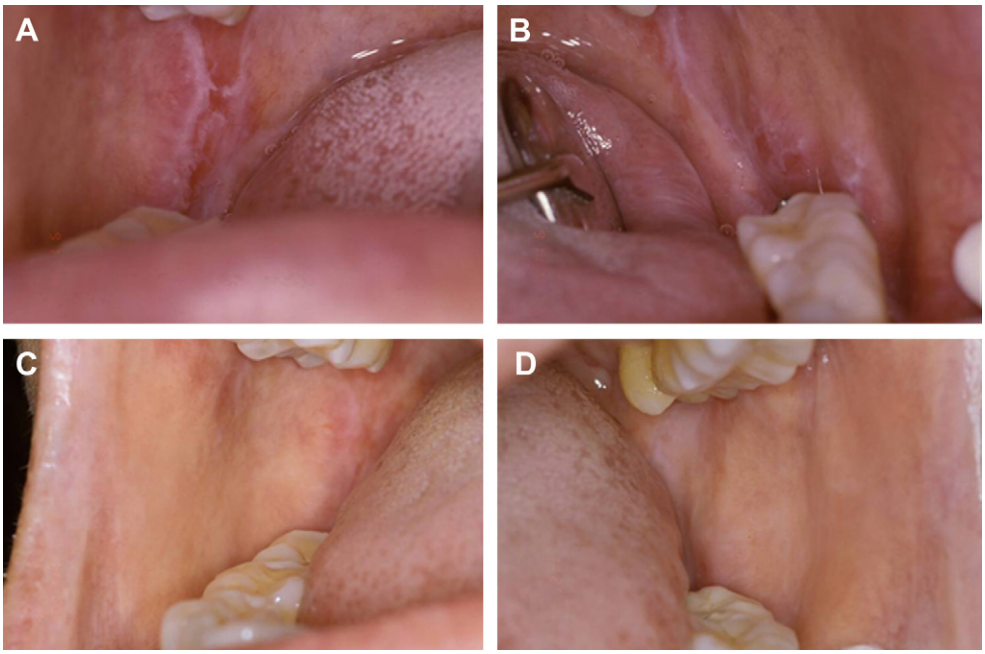

Figure 2 Clinical photographs of a patient with minor-type erosive oral lichen planus (EOLP) on the bilateral posterior buccal mucosa. (A and B) Before treatment. (C and D) After two rounds of local injection of 40 mg triamcinolone acetonide once weekly plus oral administration of 15 mg prednisolone once daily for 2 weeks, showing nearly complete regression of the lesion.

Corticosteroids have well-documented anti-inflammatory and anti-immune effects. Glucocorticoids suppress the inflammatory response by inhibiting synthesis of the two main inflammatory products, prostaglandins and leukotrienes. Glucocorticoids can inhibit prostaglandin synthesis at the level of both phospholipase A2 and cyclooxygenaseisomerase.[8] Furthermore, glucocorticoids are able to prevent the transcription of pro-inflammatory genes, including interleukins(IL) IL-1B, IL-4, IL-5, and IL-8, chemokines, cytokines, granulocyte-macrophage colony-stimulating factor, and tumor necrosis factor-α genes.[9] Glucocorticoids also suppress cell-mediated immunity. They act by inhibiting genes that code for the cytokines IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-8 and interferon-γ, the most important of which is IL-2 which is a potent T cell growth factor. Smaller cytokine production in turn reducesT-cell-proliferation.[10] As stated before, OLP is a T-cell-mediated chronic inflammatory oral mucosal disease and corticosteroids have both anti-inflammatory and anti-T cell-mediated immune functions. Therefore, it is easy to understand why local injection and systemic administration of corticosteroid can result in the accelerated healing of erosive and ulcerative oral lesions in EOLP patients.

Conventional EOLP therapies are primarily aimed at healing erosive and ulcerative EOLP lesion and relieving oral mucosal pain and burning sensation. The available treatments for EOLP consist of topical and systemic corticosteroids, retinoids, calcineurin inhibitors such as cyclosporine, tacrolimus and pimecrolimus, as well as

Table 1 Lesion response in 30 patients with major erosive oral lichen planus (EOLP) and 20 patients with minor EOLP after 3-week treatments of local injection and oral administration of corticosteroid.

	Number of patients		
	Total	Complete response	Partial response
EOLP patients	50	45	5
Major type	30	27	3
Minor type	20	18	2

Table 2 Recurrence of erosive oral lichen planus (EOLP) lesions in 27 major EOLP and 18 minor EOLP patients with complete response after 3-week treatments of local injection and oral administration of corticosteroid.

Duration (mo)	Number of patients		
	Total ($n = 45$)	Major EOLP ($n = 27$)	Minor EOLP ($n = 18$)
3	2	1	1
4	2	1	1
6	3	2	1
8	4	2	2
9	6	4	2
10	6	4	2
12	5	3	2
14	1	0	1
15	5	3	2
16	1	1	0
18	4	2	2
20	1	1	0
21	3	2	1
24	2	1	1

extracorporeal photochemotherapy. Among these treatment modalities, topical corticosteroids have been used as the first-line drugs, while systemic corticosteroids are usually reserved for widespread EOLP or acute exacerbation.[1,2] Topical application of corticosteroids could not maintain a high local corticosteroid concentration for a period long enough to promote the healing of erosive and ulcerative oral lesion. Furthermore, in order to obtain a high local corticosteroid concentration by oral administration of corticosteroid, a large dose of corticosteroid would need to be given to the patients. Therefore we used local injection of triamcinolone acetonide to achieve a high and relatively long-lasting local corticosteroid level in a short period of time. We suggest that our EOLP treatment protocol not only hastens the healing of erosive and ulcerative oral lesion in a short period of 2—3 weeks, but also frees the EOLP patients from long-term oral mucosal discomfort and gives a relatively long symptom-free remission period.

EOLP is a persistent, chronic inflammatory disease that frequently causes oral mucosal discomfort and is resistant to treatment. In this study, we used a local injection and oral administration of corticosteroid treatment protocol to treat 50 EOLP patients. We found that our treatment protocol could accelerate the healing of ELOP lesion and obtain a 90% complete response rate. Although complete response EOLP lesions recurred after a follow-up period of 3—24 months, EOLP patients did have an average remission period of 12 months after treatment with our protocol. In addition, the recurrence EOLP lesion could acquire the same clinical outcome as before when treated with the same protocol. Therefore, we suggest that our newly developed local injection and oral administration of corticosteroid treatment protocol may be a promising treatment modality for EOLP in the future.

References

1. Sugerman PB, Savage NW, Walsh LJ, Zhao ZZ, Zhou XJ, Khan A, et al. The pathogenesis of oral lichen planus. *Crit Rew Oral Biol Med* 2002;**13**:350—65.
2. Roopashree MR, Gondhalekar RV, Shashikanth MC, George J, Thippeswamy SH, Shukla A. Pathogenesis of oral lichen planus — a review. *J Oral Pathol Med* 2010;**39**:729—34.
3. Zhao ZZ, Savage NW, Sugerman PB, Walsh LJ. Mast cell/T cell interactions in oral lichen planus. *J Oral Pathol Med* 2002;**31**: 189—95.
4. Khan A, Farah CS, Savage NM, Walsh LJ, Harbrow DJ, Sugerman PB. Th1 cytokines in oral lichen planus. *J Oral Pathol Med* 2003;**32**:77—83.
5. Hirota J, Osaki T, Tatemoto Y. Immunohistochemical staining of infiltrates in oral lichen planus. *Path Res Pract* 1990;**186**: 625—32.
6. Yamamoto T, Yoneda K, Ueta E, Osaki T. Cellular immunosuppression in oral lichen planus. *J Oral Pathol Med* 1990;**19**: 464—70.
7. Sun A, Chia JS, Chang YF, Chiang CP. Serum interleukin-6 level is a useful marker in evaluating therapeutic effects of levamisole and Chinese medicinal herbs on patients with oral lichen planus. *J Oral Pathol Med* 2002;**31**:196—203.
8. Goppelt-Struebe M, Wolter D, Resch K. Glucocorticoids inhibit prostaglandin synthesis not only at the level of phospholipase A2 but also at the level of cyclo-oxygenase/PGE isomerase. *Br J Pharmacol* 1989;**98**:1287—95.
9. Newton R. Molecular mechanisms of glucocorticoid action: what is important? *Thorax* 2000;**55**:603—13.
10. Leung DYM, Bloom JW. Update on glucocorticoid action and resistance. *J Allergy Clin Immunol* 2003;**111**:3—22.